

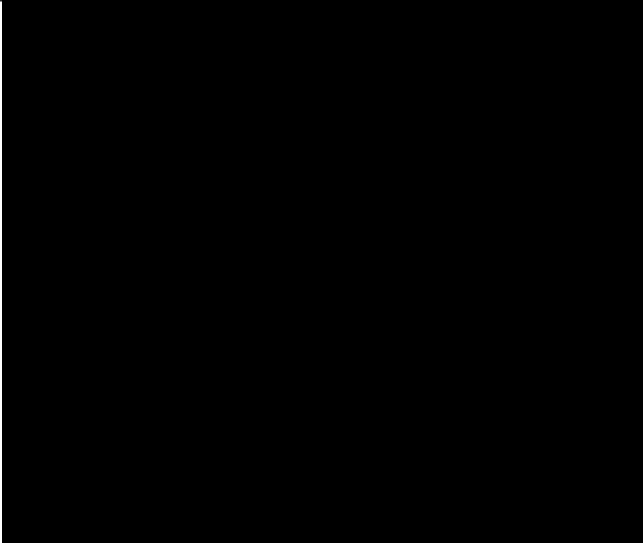
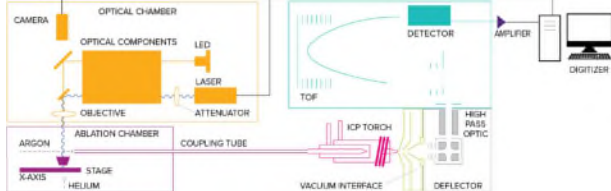
**REFILED PURSUANT TO COURT ORDER (DKT. 102)**

# **EXHIBIT F**

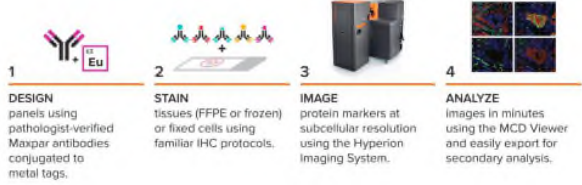
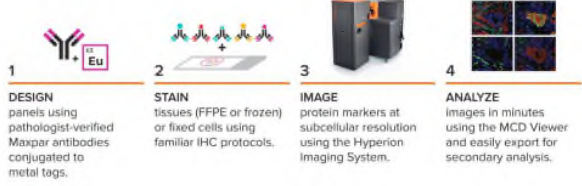
## REFILED PURSUANT TO COURT ORDER (DKT. 102)

<p><b>'386 Patent</b></p>	<p><b>Hyperion™ Instrument with Maxpar® Reagents</b></p> <p>interface (green) high-pass ion optics (gray), ion separation in the time-of-flight (TOF) mass analyzer (blue), and data acquisition and processing (red).</p>
<p><b>'104 Patent</b></p> <p>1. A method for the analysis of an analyte in a sample, comprising:</p> <p>(i) incubating an element tagged affinity reagent with an analyte, the element tagged affinity reagent comprising an affinity reagent tagged with an element tag, the element tag comprising a linear or branched polymer having multiple metal-binding pendant groups, wherein each pendant group includes at least one metal atom or is capable of binding at least one metal atom, and wherein the affinity reagent specifically binds with the analyte, wherein the analyte is located within or on an intact cell;</p> <p>(ii) separating unbound element tagged affinity reagent from bound element tagged affinity reagent; and</p> <p>(iii) analyzing the element tag bound to the affinity reagent attached to the analyte of the intact cell by atomic spectroscopy, wherein analyzing occurs without prior acidification of the sample.</p>	<p><b>Hyperion™ Instrument with Maxpar® Reagents</b></p> <p><i>The Hyperion™ Instrument with Maxpar® Reagents practices Claim 1 of the '104 Patent. For example, the Hyperion Imaging System enables cellular profiling within tissue. The Hyperion IMC Staining Protocol describes incubation with Maxpar antibodies (affinity reagent) follow by a wash step as recited in steps (i) and (ii) respectively of claim 1. Analysis is performed on the ICP-MS Helios system, as shown in Figure 3 of the Hyperion Imaging System User Guide.</i></p> <p><b><u>Pg. 3 of Hyperion IMC Staining Protocol</u></b></p> <p><b>13</b> To prepare the antibody cocktail, calculate the total volume of antibodies at concentrations specific for the assay and bring the volume up to a final volume of 0.5% BSA in Maxpar PBS. Place the slides in a hydration chamber and pipette the antibody master mix onto the section.</p> <p><b>NOTE</b></p> <ul style="list-style-type: none"> <li>• When using Fluidigm pathologist-verified Maxpar antibodies for imaging, consult the technical data sheets for the recommended dilution ranges for individual antibodies.</li> <li>• Spin the antibody at 13,000 x g for 2 minutes and pipet from the top of the tube to avoid antibody aggregates.</li> <li>• Add a small volume of individual antibodies into a larger volume of 3% BSA in Maxpar PBS diluent.</li> <li>• BSA should be 0.5% concentration in the final antibody cocktail.</li> <li>• The final volume of antibody cocktail needed depends on the size and location of your tissue sections and the number of slides. Determine volume empirically.</li> </ul> <p><b>IMPORTANT</b> It is recommended that you store the antibody cocktail on ice and add it to your samples within 1–2 hours of preparation for best results.</p> <p><b>14</b> Incubate overnight with the antibody cocktail at 4 °C in a hydration chamber. (See Step 12)</p> <p><b>15</b> Wash the slides in 0.2% Triton X-100 in Maxpar PBS for 8 minutes with slow agitation in Coplin jars. Repeat.</p> <p><b><u>Fluidigm Imaging Mass Cytometry Applications (Webpage)</u></b></p> <p>A Simple Four-Step Workflow</p> <p>The Imaging Mass Cytometry workflow enables deep profiling of standard FFPE or frozen tissue sections and of fixed cells deposited on glass microscope slides using the Hyperion Imaging System.</p> <div data-bbox="906 1493 1484 1675"> </div>

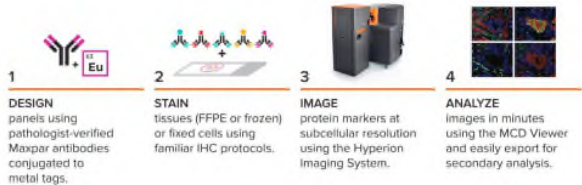
## REFILED PURSUANT TO COURT ORDER (DKT. 102)

'104 Patent	Hyperion™ Instrument with Maxpar® Reagents
	 <p data-bbox="894 766 1292 800"><b><u>Pg. 7-8 of Hyperion User Guide</u></b></p> <p data-bbox="894 806 1068 835"><b><u>Introduction</u></b></p> <p data-bbox="894 856 1502 1031">The Hyperion™ Imaging System is a mass cytometry-based high-resolution laser ablation system that allows the highly multiplexed imaging with 135 channels available. The system is designed to detect metal-tagged antibodies bound to the cell surface and intracellular proteins in tissue sections using immunohistochemical methods. This allows researchers to investigate cellular subpopulations and cell-to-cell interactions in various tissue microenvironments with greater resolution. The system allows for high-resolution cellular profiling in spatial proximity, enabling detection of disease cells and immune cells populations within the context of the tissue structure.</p> <p data-bbox="894 1045 1287 1077"><i>Single cells are profiled in tissue.</i></p> <p data-bbox="894 1108 1281 1138"><b><u>Hyperion Imaging System Technology</u></b></p> <p data-bbox="894 1155 1502 1323">The Hyperion Imaging System technology is an innovative system based on laser ablation technology coupled with mass cytometry time-of-flight (TOF) of the resulting ablation plume (see Figures 2 and 3). The Hyperion Tissue Imager uses a solid-state laser with a laser beam directed at the slide through the Sampler Cone. The sample on the slide or the tuning film on the slide is ablated and aerosolized. The ablation chamber, which houses the glass slide, is pressurized with helium and the resulting aerosol plume is delivered through the coupling tubing to the inductively coupled plasma (ICP) torch of the Helios through the argon and helium flow.</p> <p data-bbox="894 1335 1408 1365"><i>Analysis is performed on the Helios system.</i></p> <p data-bbox="894 1400 1520 1432"><b><u>Figure 3 and Description in Hyperion User Guide</u></b></p>  <p data-bbox="894 1638 1526 1698"><b>Figure 3. Schematic of the Hyperion Imaging System coupled to the Helios instrument</b></p>
<p data-bbox="272 1707 855 1869">2. The method of claim 1, wherein incubating the element tagged affinity reagent with the analyte comprises: incubating two or more differential element tagged affinity reagents with two or more</p>	<p data-bbox="894 1707 1520 1869"><i>The Hyperion™ Instrument with Maxpar® Reagents practices Claim 2 of the '104 Patent. For example, the workflow depicted on the Fluidigm Mass Cytometry Methods (Webpage) describes use of multiple metal (element) tagged antibodies.</i></p>

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'104 Patent	Hyperion™ Instrument with Maxpar® Reagents
<p>analytes, wherein the element tagged affinity reagents specifically bind with the two or more analytes to produce two or more differentially tagged analytes, wherein analyzing the element tag bound to the affinity reagent comprises analyzing the differential element tags bound to the two or more analytes by atomic spectroscopy.</p>	<p><b><u>Fluidigm Imaging Mass Cytometry Applications (Webpage)</u></b></p> <p>A Simple Four-Step Workflow</p> <p>The Imaging Mass Cytometry workflow enables deep profiling of standard FFPE or frozen tissue sections and of fixed cells deposited on glass microscope slides using the Hyperion Imaging System.</p> 
<p>14. The method of claim 1, wherein the affinity reagent is an antibody.</p>	<p><i>The Hyperion™ Instrument with Maxpar® Reagents practices Claim 14 of the '104 Patent. For example, the workflow depicted on the Fluidigm Imaging Mass Cytometry Applications (Webpage) describes use of antibody affinity reagents.</i></p> <p><b><u>Fluidigm Imaging Mass Cytometry Applications (Webpage)</u></b></p> <p>A Simple Four-Step Workflow</p> <p>The Imaging Mass Cytometry workflow enables deep profiling of standard FFPE or frozen tissue sections and of fixed cells deposited on glass microscope slides using the Hyperion Imaging System.</p> 
'698 Patent	Hyperion™ Instrument with Maxpar® Reagents
<p>1. A system for sequentially analyzing single cells in a sample by mass spectrometry, wherein the sample comprises a plurality of tagged cells tagged with a plurality of tagged antibodies, wherein each of the plurality of tagged antibodies is specific for a different analyte, and wherein each of the plurality of tagged antibodies is tagged with an elemental tag comprising a lanthanide or noble metal; wherein the system comprises: a first device to vaporize, atomize, and ionize multiple elemental tags from a single first cell of the plurality of tagged cells and multiple elemental tags from a single second cell of the plurality of tagged cells; and</p>	<p><i>The Hyperion™ Instrument with Maxpar® Reagents practices Claim 1 of the '698 Patent. For example, the Fluidigm Imaging Mass Cytometry Applications webpage and the Hyperion User Guide describe a sample comprising metal tagged antibodies, and a system to vaporize, atomize, and ionize multiple elemental tags (by directing LA-plumes to the ICP torch) and detecting by mass spectrometry (by TOF-MS).</i></p> <p><b><u>Fluidigm Imaging Mass Cytometry Methods (Webpage)</u></b></p>

## REFILED PURSUANT TO COURT ORDER (DKT. 102)

'698 Patent	Hyperion™ Instrument with Maxpar® Reagents
<p>a second device to detect, by mass spectrometry, lanthanides and/or noble metals of the single first cell by detecting a transient signal of the multiple vaporized, atomized, and ionized elemental tags of the single first cell, and lanthanides and/or noble metals of the single second cell by detecting a transient signal of the multiple vaporized, atomized, and ionized elemental tags of the single second cell, wherein the transient signal associated with the single first cell and the transient signal associated with the single second cell are detected sequentially.</p>	<p>A Simple Four-Step Workflow</p> <p>The Imaging Mass Cytometry workflow enables deep profiling of standard FFPE or frozen tissue sections and of fixed cells deposited on glass microscope slides using the Hyperion Imaging System.</p>  <p><b>Pg. 7 of Hyperion User Guide</b></p> <p><b>Introduction</b></p> <p>The Hyperion™ Imaging System is a mass cytometry-based high-resolution laser ablation system that allows the highly multiplexed imaging with 135 channels available. The system is designed to detect metal-tagged antibodies bound to the cell surface and intracellular proteins in tissue sections using immunohistochemical methods. This allows researchers to investigate cellular subpopulations and cell-to-cell interactions in various tissue microenvironments with greater resolution. The system allows for high-resolution cellular profiling in spatial proximity, enabling detection of disease cells and immune cells populations within the context of the tissue structure.</p> <p><i>Single cells are profiled in tissue.</i></p> <p><b>Pg. 9 of Hyperion User Guide</b></p> <p>The system directs a pulsed laser beam through the optical components of the optics chamber through the attenuator, which functions to moderate the energy of the laser. The camera captures the image from the slide that has been loaded onto the stage of the ablation chamber. The laser beam ablates spots on the slide, resulting in plumes of aerosol particles (ablated material). The plumes are directed to the Helios ICP torch, where they are vaporized, atomized, and ionized in the plasma. The high-pass optic removes the low-mass ions, resulting in an ion cloud that enters the TOF mass analyzer. The ions are separated</p> <p><b>Figure 3 and Description in Hyperion User Guide</b></p>  <p><i>Figure 3. Schematic of the Hyperion Imaging System coupled to the Helios instrument</i></p>
<p>5. The system of claim 1, wherein at least one of the plurality of tagged antibodies is tagged using diethylenetriaminepentaacetic acid anhydride (DTPA), 1,4,7,10-tetraazacyclododecanetetraacetic acid (DOTA), or a derivative thereof.</p>	<p><i>The Hyperion™ Instrument with Maxpar® Reagents practices Claim 1 of the '698 Patent. For example, the Maxpar X8 Polymer comprises DTPA.</i></p>

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'698 Patent	Hyperion™ Instrument with Maxpar® Reagents

6. The system of claim 1, wherein each of the plurality of tagged antibodies is tagged with a distinct isotope.

*The Hyperion™ Instrument with Maxpar® Reagents practices Claim 6 of the '698 Patent. For example, 74 antibody labeling kits and labeled antibodies for Hyperion (some shown below) are sold by Fluidigm, all of which have isotope tags.*

### Maxpar Antibody Listing for Hyperion

Imaging-optimized Maxpar antibodies for human FFPE tissues

Target	Catalog Number	Clone	Tag	Format	Target	Catalog Number	Clone	Tag	Format
Alpha-SMA	314107D	1A4	149y	25 µg	CD16	3146020D	EP016784	146Nd	25 µg
Arginase 1	3164027D	D4E3M	164Dy	25 µg	CD19	3142014D	6CMP31	142Nd	25 µg
BT-H4	3166030D	H74	166Er	25 µg	CD20	3168029D	H1	168Dy	25 µg
BCL-2	3146019D	EP017509	146Nd	25 µg	CD25	3175036D	EP06452	175Lu	25 µg
BCL-6	3147020D	K112-91	147Sm	25 µg	CD27	3178024D	EP08569	171Yb	25 µg
Beta-actin	3154021D	2F11	154Sm	25 µg	CD31	3158025D	EP03094	158Eu	25 µg
Beta-catenin	3155032D	D13A1	155Ho	25 µg	CD33	3145040D	Polyclonal	145Nd	25 µg
BRCA1	3172030D	MS90	172Yb	25 µg	CD38	3141018D	EP04106	141Pr	25 µg
C-Myc p67	3164025D	9E10	164Dy	25 µg	CD44	3153029D	IM7	153Eu	25 µg
Caspase-3 cleaved	3172027D	5A1E	172Yb	25 µg	CD45	3152016D	CD45-2B11	152Sm	25 µg
CD3	3170019D	Polyclonal, C-Terminal	170Er	25 µg	CD45	3152018D	DGM81	152Sm	25 µg
CD4	3155033D	EP06855	156Gd	25 µg	CD45RA	3166028D	HN00	166Er	25 µg
CD8a	3162034D	C8/144B	162Dy	25 µg	CD45RO	3173016D	UCHL1	173Yb	25 µg
CD8a	3162035D	D8A8Y	162Dy	25 µg	CD63	3150029D	H5C6	150Nd	25 µg
CD11b	3140028D	EP01344	140Sm	25 µg	CD66a	3170020D	CD66a-B11	171Yb	25 µg
CD11c	3154025D	Polyclonal	154Sm	25 µg	CD68	3159035D	KP1	159Tb	25 µg
CD14	3144025D	EP03653	144Nd	25 µg	CD73	3158039D	EP06195	158Gd	25 µg
CD15	3140026D	W6D3	140Sm	25 µg	CD74	3166025D	LN2	166Er	25 µg
					CD107a/LAMP1	3158021D	H4A3	158Eu	25 µg

*The tag column shows use of isotopic elements, with isotope mass represented by the numbers preceding the letters identifying the element.*

Fluidigm's investigation is ongoing and Fluidigm reserves the right to supplement its objections and/or its response to this Interrogatory, including (without limitation) at appropriate times set forth in a Scheduling Order entered by the Court.

### INTERROGATORY NO. 9